ATTACHMENT 4

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 20-938/S-013, S-015
NDA 21-530/S-001, S-003

Boehringer Ingelheim Pharmaceuticals, Inc.
900 Ridgebury Road/P.O. Box 368
Ridgefield, CT 06877-0368

Attention: Charles R. Mazzarella
Associate Director, Drug Regulatory Affairs

Dear Mr. Mazzarella:

Please refer to your supplemental new drug applications dated February 18, 2005, received February 18, 2005 (NDA 20-938/S-013 and NDA 21-530/S-001), and dated July 14, 2005, received July 15, 2005 (NDA 20-938/S-015 and NDA 21-530/S-003), submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Mobic® (meloxicam) Tablets and Mobic® (meloxicam) Oral Suspension.

We acknowledge receipt of your submissions dated April 11, May 2 and 18, June 10, 16, 17, and 27, July 21, and August 10, 2005 (NDA 20-938/S-013 and NDA 21-530/S-001), and your submission dated August 5, 2005, (NDA 20-938/S-015 and NDA 21-530/S-003.)

Supplements S-013 (N 20-938) and S-001 (N 21-530) provide for the use of Mobic® (meloxicam) Tablets and Mobic Oral Suspension for relief of the signs and symptoms of pauciarticular or polyarticular course Juvenile Rheumatoid Arthritis in patients 2 years of age and older.

Supplements S-015 (N 20-938) and S-003 (N 21-530) provide for the revised package insert to include a boxed warning, additional information about cardiovascular risks, and a MedGuide as requested by the Agency in the June 14, 2005, letter.

We have completed our review of these applications, as amended, and they are approved, effective on the date of this letter, for use as recommended in the agreed-upon labeling text.

The final printed labeling (FPL) must be identical to the package insert and MedGuide submitted August 10, 2005.

Please submit an electronic version of the FPL according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format - NDA*. Alternatively, you may submit 20 paper copies of the FPL as soon as it is available but no more than 30 days after it is printed. Individually mount 15 of the copies on heavy-weight paper or similar material. For administrative purposes, designate these submissions "**FPL for approved supplements NDA 20-938/S-013, S-015 and NDA 21-530/S-001, S-003.**" Approval of these submissions by the FDA is not required before the labeling is used.

All applications for new active ingredients, new dosage forms, new indications, new routes of administration, and new dosing regimens are required to contain an assessment of the safety and effectiveness of the product in pediatric patients unless this requirement is waived or deferred. We note that you have fulfilled the pediatric study requirement for this application.

In addition, submit three copies of the introductory promotional materials that you propose to use for these products. Submit all proposed materials in draft or mock-up form, not final print. Send one copy to the Division of Anesthesia, Analgesia and Rheumatology Products and two copies of both the promotional materials and the package inserts directly to:

Division of Drug Marketing, Advertising, and Communications, HFD-42
Food and Drug Administration
5600 Fishers Lane
Rockville, MD 20857

If you issue a letter communicating important information about this drug product (i.e., a "Dear Health Care Professional" letter), we request that you submit a copy of the letter to this NDA and a copy to the following address:

MEDWATCH, HFD-410
FDA
5600 Fishers Lane
Rockville, MD 20857

Effective August 29, 2005, **ALL** regulatory submissions, whether sent by U.S. Postal Service, an overnight mail service, or courier, should be sent to the following address. Processing of submissions sent to other addresses may be delayed.

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Anesthesia, Analgesia and Rheumatology Products
5901-B Ammendale Road
Beltsville, MD 20705-1266

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

If you have any questions, call Constantine J. Markos, Pharm.D., Regulatory Health Project Manager, at (301) 827-2496.

Sincerely,

{See appended electronic signature page}

Bob Rappaport, M.D.
Director
Division of Anesthesia, Analgesia
and Rheumatology Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

Enclosure

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/s/

Sharon Hertz
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Signing for Bob Rappaport, MD

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 20-938/S-004

Boehringer Ingelheim Pharmaceuticals, Inc.
Attention: Jeffery R. Snyder
Senior Associate Director
Drug Regulatory Affairs
900 Ridgebury, Road
Ridgefield, CT 06877

Dear Mr. Snyder:

Please refer to your supplemental new drug application dated February 28, 2001, received February 28, 2001, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Mobic® (meloxicam) Tablets, 7.5 mg and 15 mg.

We acknowledge receipt of your submissions dated December 20, 2001; January 18, and February 05, 2002; January 15, February 10, and 26, May 26, and June 18, 2004. Your submission of January 15, 2004 constituted a complete response to our December 21, 2001 action letter.

This supplemental new drug application provides for the use of Mobic® (meloxicam) Tablets, 7.5 mg and 15 mg for the relief of the signs and symptoms of rheumatoid arthritis in adults.

We completed our review of this application, as amended. This application is approved, effective on the date of this letter, for use as recommended in the agreed-upon labeling text.

The final printed labeling (FPL) must be identical to the enclosed labeling.

The electronic labeling rule published December 11, 2003, (68 FR 69009) requires submission of labeling content in electronic format effective June 8, 2004. For additional information, consult the following guidances for industry regarding electronic submissions: *Providing Regulatory Submissions in Electronic Format - NDAs* (January 1999) and *Providing Regulatory Submissions in Electronic Format – Content of Labeling* (February 2004). The guidances specify that labeling to be submitted in *pdf* format. To assist in our review, we request that labeling also be submitted in MS Word format. If formatted copies of all labeling pieces (i.e., package insert, patient package insert, container labels, and carton labels) are submitted electronically, labeling does not need to be submitted in paper.

All applications for new active ingredients, new dosage forms, new indications, new routes of administration, and new dosing regimens are required to contain an assessment of the safety and effectiveness of the product in pediatric patients unless this requirement is waived or deferred. We are waiving the pediatric study requirement for ages 0 to < 2 years and deferring pediatric studies for ages 2 years to 17 years for this application.

Your deferred pediatric studies required under section 2 of the Pediatric Research Equity Act (PREA) are considered required postmarketing study commitments. The status of these postmarketing studies shall be reported annually according to 21 CFR 314.81. This commitment is listed below.

1. Deferred pediatric study under PREA for the treatment of juvenile rheumatoid arthritis in pediatric patients ages 2 years to 17 years.

   Final Report Submission: January 31, 2005

Submit final study reports to this NDA. For administrative purposes, all submissions related to this pediatric postmarketing study commitment must be clearly designated "**Required Pediatric Study Commitments**".

In addition, submit three copies of the introductory promotional materials that you propose to use for this product. Submit all proposed materials in draft or mock-up form, not final print. Send one copy to the Division of Anti-Inflammatory, Analgesic, & Ophthalmic Drug Products and two copies of both the promotional materials and the package insert directly to:

Division of Drug Marketing, Advertising, and Communications, HFD-42
Food and Drug Administration
5600 Fishers Lane
Rockville, MD 20857

If you issue a letter communicating important information about this drug product (i.e., a "Dear Health Care Professional" letter), we request that you submit a copy of the letter to this NDA and a copy to the following address:

MEDWATCH, HFD-410
FDA
5600 Fishers Lane
Rockville, MD 20857

Please submit one market package of the drug product when it is available. We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

If you have any questions, call Barbara Gould, Regulatory Project Manager, at (301) 827-2506.

Sincerely,

{See appended electronic signature page}

Brian E. Harvey, M.D., Ph.D.
Acting Director
Division of Anti-Inflammatory, Analgesic, &
Ophthalmic Drug Products
Office of Drug Evaluation V
Center for Drug Evaluation and Research

Enclosure

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/s/

Brian Harvey
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DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-530

Boehringer Ingelheim Pharmaceutical, Inc.
Attention: Charles Mazzarella
Manager, Drug Regulatory Affairs
900 Ridgebury Road
P.O. Box 368
Ridgefield, CT 06877

Dear Mr. Mazzarella:

Please refer to your new drug application (NDA) dated August 18, 2003, received August 19, 2003, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Mobic® Oral Suspension (meloxicam oral suspension), 7.5 mg/5 mL.

We acknowledge receipt of your submissions dated October 29, and December 18, 2003; and January 21, February 13, and 25, March 12, April 13, 26, and 28, and May 10, 12, and 18, 2004.

This new drug application provides for the use of Mobic® Oral Suspension (meloxicam oral suspension) 7.5 mg/5 mL for the relief of the signs and symptoms of osteoarthritis.

We completed our review of this application, as amended. It is approved, effective on the date of this letter, for use as recommended in the agreed-upon labeling text.

The final printed labeling (FPL) must be identical to the enclosed labeling (text for the package insert) and submitted labeling package insert submitted May 10, 2004, and the (immediate container and carton labels submitted August 18, 2003). Marketing the product(s) with FPL that is not identical to the approved labeling text may render the product misbranded and an unapproved new drug.

Please submit an electronic version of the FPL according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format - NDA*. Alternatively, you may submit 20 paper copies of the FPL as soon as it is available but no more than 30 days after it is printed. Individually mount 15 of the copies on heavy-weight paper or similar material. For administrative purposes, designate this submission "**FPL for approved NDA 21-530.**" Approval of this submission by FDA is not required before the labeling is used.

All applications for new active ingredients, new dosage forms, new indications, new routes of administration and new dosing regimens are required to contain an assessment of the safety and effectiveness of the product in pediatric patients unless this requirement is waived or deferred. We are waiving the pediatric study requirement for this application.

In addition, submit three copies of the introductory promotional materials that you propose to use for this product. Submit all proposed materials in draft or mock-up form, not final print. Send one copy to

the Division of Anti-Inflammatory, Analgesic, and Ophthalmic Drug Products and two copies of both the promotional materials and the package insert directly to:

Division of Drug Marketing, Advertising,
and Communications, HFD-42
Food and Drug Administration
5600 Fishers Lane
Rockville, MD 20857

Please submit one market package of the drug product when it is available.
We have not completed validation of the regulatory methods. However, we expect your continued cooperation to resolve any problems that may be identified.

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

If you have any questions, call Barbara Gould, Regulatory Project Manager, at (301) 827-2506.

Sincerely,

{See appended electronic signature page}

Brian E. Harvey, M.D., Ph.D.
Acting Director
Division of Anti-Inflammatory, Analgesic, &
Ophthalmic Drug Products
Office of Drug Evaluation V
Center for Drug Evaluation and Research

Enclosure

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/s/

Brian Harvey
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NDA 20-938

Boehringer Ingelheim Pharmaceuticals, Inc.
Attention: Martin M. Kaplan, M.D., J.D.
900 Ridgebury Road
P.O. Box 368
Ridgefield, CT 06877-0368

Dear Dr. Kaplan:

Please refer to your new drug application (NDA) dated December 15, 1998, received December 16, 1998, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Mobic (meloxicam) Tablets 7.5 mg.

We acknowledge receipt of your submissions dated January 31, February 11, and February 28, March 27, April 3, April 10, and April 13, 2000. Your submission of February 11, 2000 constituted a complete response to our December 15, 1999 action letter.

This new drug application provides for the use of Mobic (meloxicam) Tablets 7.5 mg for relief of the signs and symptoms of osteoarthritis.

We have completed the review of this application, as amended, and have concluded that adequate information has been presented to demonstrate that the drug product is safe and effective for use as recommended in the agreed upon enclosed labeling text. Accordingly, the application is approved effective on the date of this letter.

The final printed labeling (FPL) must be identical to the enclosed labeling (text for the package insert, immediate container and carton labels). Marketing the product with FPL that is not identical to the approved labeling text may render the product misbranded and an unapproved new drug.

Please submit 20 copies of the FPL as soon as it is available, in no case more than 30 days after it is printed. Please individually mount ten of the copies on heavy-weight paper or similar material. For administrative purposes, this submission should be designated "FPL for approved NDA 20-938." Approval of this submission by FDA is not required before the labeling is used.
In addition, please submit three copies of the introductory promotional materials that you propose to use for this product. All proposed materials should be submitted in draft or mock-up form, not final print. Please submit one copy to this Division and two copies of both the promotional materials and the package insert directly to:

Division of Drug Marketing, Advertising, and Communications, HFD-40
Food and Drug Administration
5600 Fishers Lane
Rockville, Maryland 20857

Please submit one market package of the drug product when it is available.

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

If you have any questions, contact Anthony M. Zeccola, Senior Regulatory Management Officer, at (301) 827-2090.

Sincerely,

Robert DeLap, M.D., Ph.D.
Director
Office of Drug Evaluation V
Center for Drug Evaluation and Research